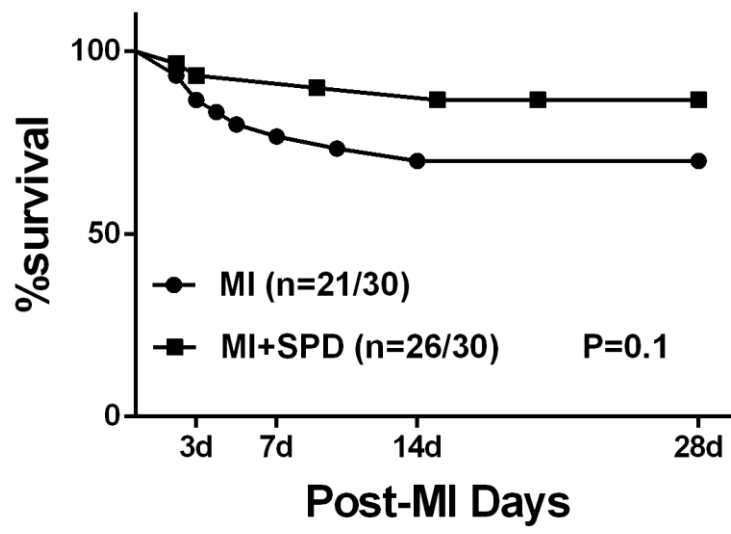
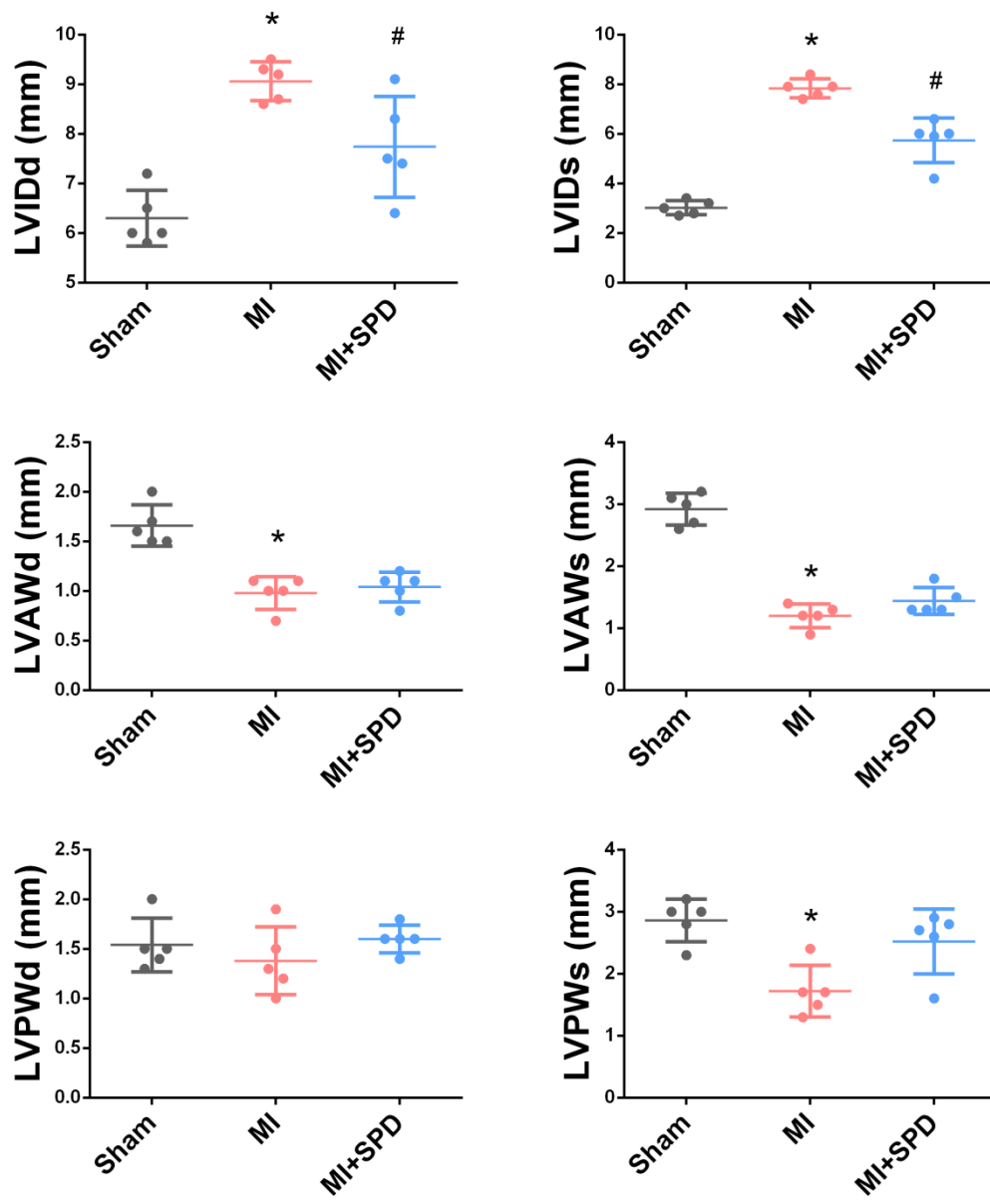


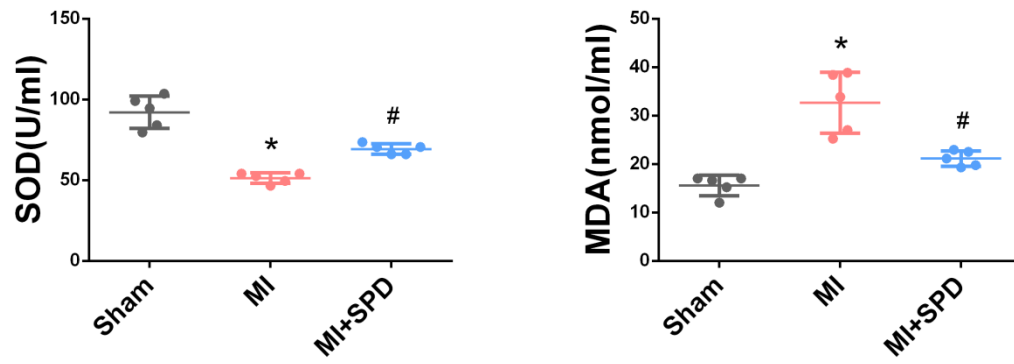
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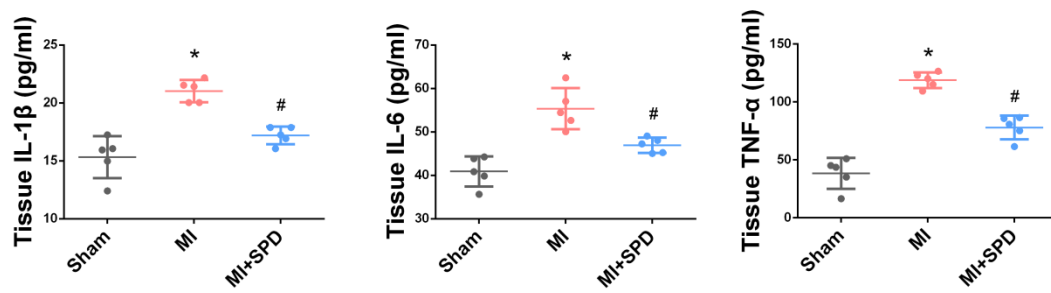
S2



S3



S4



S5

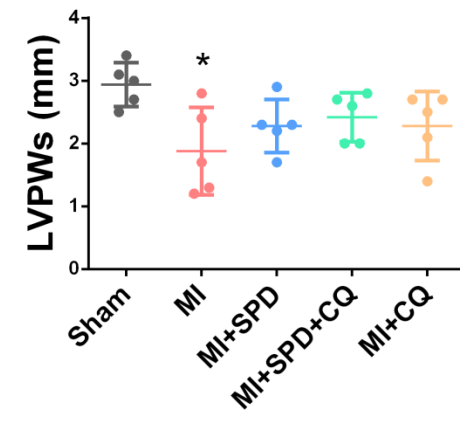
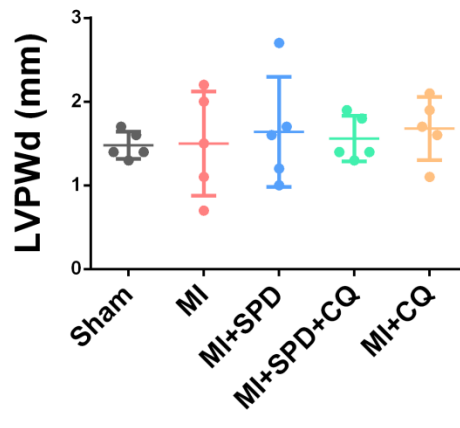
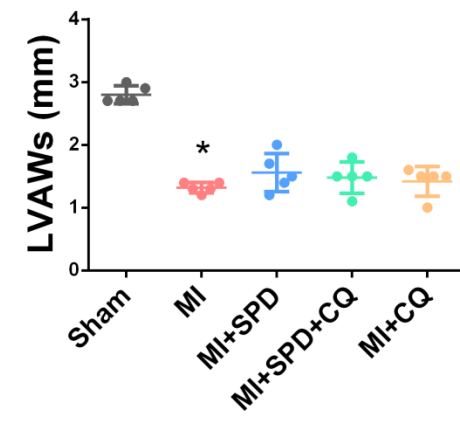
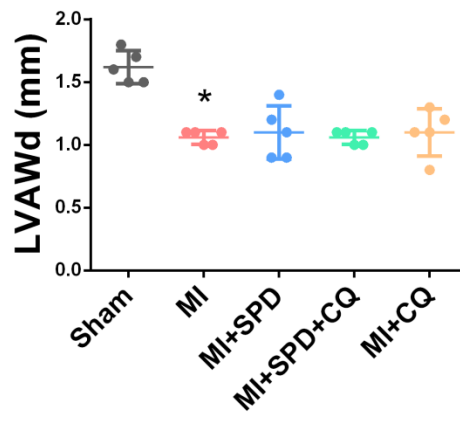
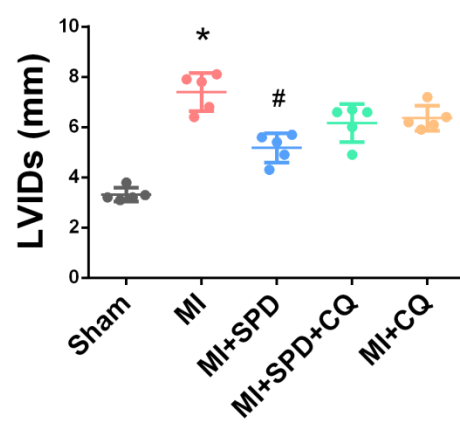
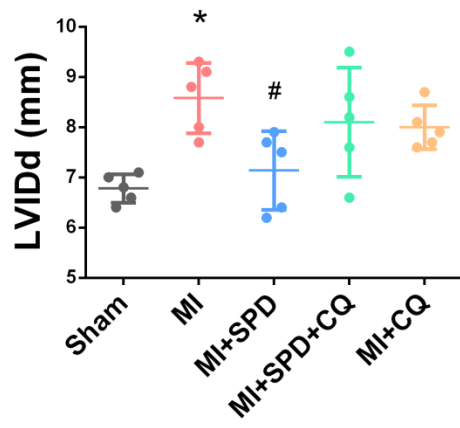


Figure S1. Survival analysis of rats with or without SPD after MI. n=30 per group. All rats in Sham group survived.

Figure S2. Echocardiography parameters were measured in each group, including left ventricular (LV) internal diameters at diastole (LVIDd; in mm), LV internal diameters at systole (LVIDs; in mm), LV anterior wall thickness at diastole (LVAWd; in mm), LV anterior wall thickness at systole (LVAWs; in mm), LV posterior wall thickness at diastole (LVPWd; in mm), LV posterior wall thickness at systole (LVPWs; in mm). n=5, * $P < 0.05$ versus sham group, # $P < 0.05$ versus MI group.

Figure S3. Measurement and quantitative analysis of SOD and MDA in rat heart tissues. n=5, * $P < 0.05$ versus sham group, # $P < 0.05$ versus MI group.

Figure S4. Measurement and quantitative analysis of inflammatory cytokines in rat heart tissues. n=5, * $P < 0.05$ versus sham group, # $P < 0.05$ versus MI group.

Figure S5. Echocardiography parameters were measured in each group, including left ventricular (LV) internal diameters at diastole (LVIDd; in mm), LV internal diameters at systole (LVIDs; in mm), LV anterior wall thickness at diastole (LVAWd; in mm), LV anterior wall thickness at systole (LVAWs; in mm), LV posterior wall thickness at diastole (LVPWd; in mm), LV posterior wall thickness at systole (LVPWs; in mm). n=5, * $P < 0.05$ versus sham group, # $P < 0.05$ versus MI group.

Supplementary Methods

1. Antibodies information

The detailed information on antibodies used for Western Blotting has been summarized as followed.

| Name | Source | cat# | RRID |
|--|---------------------------|--------|-------------|
| rabbit-anti-LC3B | Cell Signaling Technology | 2775S | AB_915950 |
| rabbit-anti-p62 | Cell Signaling Technology | 5114S | AB_10624872 |
| rabbit-anti-Bcl2 | Cell Signaling Technology | 2876S | |
| rabbit-anti-Bax | Cell Signaling Technology | 2772S | AB_10695870 |
| rabbit-anti-Caspase3 | Cell Signaling Technology | 9662S | AB_331439 |
| rabbit-anti-AMPK α | Cell Signaling Technology | 2532S | AB_330331 |
| rabbit-anti-Phospho-AMPK α (Thr172) | Cell Signaling Technology | 2535S | AB_331250 |
| rabbit-anti-mTOR | Cell Signaling Technology | 2972S | AB_330978 |
| rabbit-anti-Phospho-mTOR(Ser2448) | Cell Signaling Technology | 5536S | AB_10691552 |
| rabbit-anti-GAPDH | Bioworld Technology | AP0063 | AB_2651132 |

2. Grouping design for eliminating physiological differences

In order to rule out the influence of individual differences, all male rats with 6-8 week-old were enrolled in our experiment. Rats in same experiment were purchased from Southern Medical University with one batch. Three batches of rats have been used in our research. The weights of each rat were estimated. In addition, completely randomized grouping design was used to reduce the physiological individual differences. No differences in gender, age and weights were shown among each group. The mean weights of each groups as below:

Table 1 Weights of the 1st batch (mean \pm SD)

| Group | Number | Weight(g) |
|--------|--------|-----------------|
| Sham | 6 | 207.8 \pm 6.5 |
| MI | 8 | 208.3 \pm 4.9 |
| MI+SPD | 8 | 207.4 \pm 6.8 |

Table 2 Weights of the 2nd batch (mean \pm SD)

| Group | Number | Weight(g) |
|-----------|--------|-----------------|
| Sham | 6 | 209.8 \pm 4.4 |
| MI | 8 | 209.3 \pm 5.9 |
| MI+SPD | 8 | 210.4 \pm 5.7 |
| MI+SPD+CQ | 8 | 210.8 \pm 4.8 |
| MI+CQ | 8 | 211.4 \pm 6.2 |

Table 3 Weights of the 3rd batch (mean \pm SD)

| Group | Number | Weight(g) |
|---------------|--------|-----------------|
| Sham | 5 | 210.8 \pm 5.8 |
| MI | 8 | 211.0 \pm 5.6 |
| MI+SPD | 8 | 208.9 \pm 6.4 |
| MI+SPD+Comp C | 8 | 209.9 \pm 7.2 |

3.Post-surgical handling and analgesia and sacrifice

Penicillin was used to prevent infection, tramadol (intraperitoneal injection) was used for analgesia post-surgery under the direction of medication specification. In order to improve the living environment post ligation, all cages and foods as well as drinking water were sterilized with ultraviolet light. Animals were sacrificed by carbon dioxide inhalation as the rats were put into an aeration cage filled with CO₂ for 1-3 minutes and then died.

4.Post-surgical survival rate of rats

Three batches of rats have been used in our research and the survival rate of each batch has been attached as bellow:

Table 1 The detail survival information of the 1st batch

| Number | Groups | Days of survival | Outcomes |
|--------|----------|------------------|----------|
| 1 | Sham | 28 | survive |
| 2 | Sham | 28 | survive |
| 3 | Sham | 28 | survive |
| 4 | Sham | 28 | survive |
| 5 | Sham | 28 | survive |
| 6 | Sham | 28 | survive |
| 7 | MI group | 28 | survive |

| | | | |
|----|--------------|----|---------|
| 8 | MI group | 3 | die |
| 9 | MI group | 28 | survive |
| 10 | MI group | 28 | survive |
| 11 | MI group | 28 | survive |
| 12 | MI group | 10 | die |
| 13 | MI group | 28 | survive |
| 14 | MI group | 28 | survive |
| 15 | MI+SPD group | 28 | survive |
| 16 | MI+SPD group | 28 | survive |
| 17 | MI+SPD group | 28 | survive |
| 18 | MI+SPD group | 28 | survive |
| 19 | MI+SPD group | 4 | die |
| 20 | MI+SPD group | 28 | survive |
| 21 | MI+SPD group | 28 | survive |
| 22 | MI+SPD group | 28 | survive |

Table 2 The detail survival information of the 2nd batch

| Number | Groups | Days of survival | Outcomes |
|--------|-----------------|------------------|----------|
| 1 | Sham | 28 | survive |
| 2 | Sham | 28 | survive |
| 3 | Sham | 28 | survive |
| 4 | Sham | 28 | survive |
| 5 | Sham | 28 | survive |
| 6 | Sham | 28 | survive |
| 7 | MI group | 17 | die |
| 8 | MI group | 2 | die |
| 9 | MI group | 28 | survive |
| 10 | MI group | 28 | survive |
| 11 | MI group | 28 | survive |
| 12 | MI group | 28 | survive |
| 13 | MI group | 28 | survive |
| 14 | MI group | 7 | die |
| 15 | MI+SPD group | 12 | die |
| 16 | MI+SPD group | 28 | survive |
| 17 | MI+SPD group | 28 | survive |
| 18 | MI+SPD group | 28 | survive |
| 19 | MI+SPD group | 28 | survive |
| 20 | MI+SPD group | 28 | survive |
| 21 | MI+SPD group | 28 | survive |
| 22 | MI+SPD group | 28 | survive |
| 23 | MI+SPD+CQ group | 28 | survive |
| 24 | MI+SPD+CQ group | 28 | survive |
| 25 | MI+SPD+CQ group | 3 | die |
| 26 | MI+SPD+CQ group | 28 | survive |

| | | | |
|----|-----------------|----|---------|
| 27 | MI+SPD+CQ group | 9 | die |
| 28 | MI+SPD+CQ group | 28 | survive |
| 29 | MI+SPD+CQ group | 28 | survive |
| 30 | MI+SPD+CQ group | 28 | survive |
| 31 | MI+CQ group | 28 | survive |
| 32 | MI+CQ group | 28 | survive |
| 33 | MI+CQ group | 28 | survive |
| 34 | MI+CQ group | 28 | survive |
| 35 | MI+CQ group | 28 | survive |
| 36 | MI+CQ group | 28 | survive |
| 37 | MI+CQ group | 2 | die |
| 38 | MI+CQ group | 5 | die |

Table 3 The detail survival information of the 3rd batch

| Number | Groups | Days of survival | Outcomes |
|--------|---------------------|------------------|----------|
| 1 | Sham | 28 | survive |
| 2 | Sham | 28 | survive |
| 3 | Sham | 28 | survive |
| 4 | Sham | 28 | survive |
| 5 | Sham | 28 | survive |
| 6 | MI group | 28 | survive |
| 7 | MI group | 28 | survive |
| 8 | MI group | 2 | die |
| 9 | MI group | 28 | survive |
| 10 | MI group | 28 | survive |
| 11 | MI group | 28 | survive |
| 12 | MI group | 28 | survive |
| 13 | MI group | 11 | die |
| 14 | MI+SPD group | 3 | die |
| 15 | MI+SPD group | 28 | survive |
| 16 | MI+SPD group | 28 | survive |
| 17 | MI+SPD group | 15 | die |
| 18 | MI+SPD group | 28 | survive |
| 19 | MI+SPD group | 28 | survive |
| 20 | MI+SPD group | 28 | survive |
| 21 | MI+SPD group | 28 | survive |
| 22 | MI+SPD+Comp C group | 28 | survive |
| 23 | MI+SPD+Comp C group | 28 | survive |
| 24 | MI+SPD+Comp C group | 28 | survive |
| 25 | MI+SPD+Comp C group | 28 | survive |
| 26 | MI+SPD+Comp C group | 28 | survive |
| 27 | MI+SPD+Comp C group | 4 | die |
| 28 | MI+SPD+Comp C group | 28 | survive |
| 29 | MI+SPD+Comp C group | 8 | die |

5.Stability of animal model

In order to ensure the stability of animal model, several measures were taken as followed: 1) Experimental rats were from one batch and the LAD ligation surgery was operated by one experienced and professional surgeon at the same period; 2) the ligation site was strictly limited at 2mm far from the lower margin of left auricle and ischemia features, including the color of infarcted region turned from red to pale and heart rates slowed were obviously shown; 3) After ligation, ECG were performed immediately to ensure the elevation of ST segment; 4) In our pre-experiment, echocardiographic and Masson staining were performed in some rats to estimate the equivalence of cardiac systolic function and infarction size after ligation and the results revealed that equivalence between each rats, which demonstrated that our animal models were stable.

In conclusion, it is reasonable for us to confirm that the area at risk in all the rats is equivalent between groups.

6.Administration method of SPD

First of all, the administration method of SPD was based on two related literatures (*Michiels C, Kurdi A, Timmermans J, Atherosclerosis; Eisenberg T, Abdellatif M, Schroeder S, Nat.Med*), in which SPD was dissolved into drinking water and all rats were given sufficient and free drinking water. According to the research of the *Eisenberg et al Nature Medicine 2016*, after given adequate drinking water with 3mM SPD for 2 weeks, rats' plasma levels of SPD remained in a stable range and significantly higher than those with regular water. Therefore, we believed that SPD supplement by given sufficient and free drinking water can make each rat maintain a relatively stable SPD plasma concentration which is also the effective concentration. Secondly, in our pre-experiment, we have estimated the average daily water intake of each rat by using metabolic cages and the results revealed that the general water intake of each rat was almost the same, namely around 50 ml/day. Taken together, these results suggested that after given free drinking water with SPD, the plasma

levels of SPD in rats would maintain a stable range and exerted effects.

According to the findings of *Martinet W et al Atherosclerosis 2016* in which 5mM SPD in drinking water for mice 4 weeks exerts protection in vascular disease. In our study, SPD supplement period is 4 weeks which was consistent with that in *Martinet W et al Atherosclerosis 2016*. Therefore, we decided to use 5mM SPD to perform the study.